

Docket No.: 4614-0197PUS1  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Peter Birk RASMUSSEN et al.

Application No.: 10/577,489

Confirmation No.: 5111

Filed: April 27, 2006

Art Unit: N/A

For: METHOD FOR DOWN-REGULATION OF  
VEGF

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT**  
**(SUBMISSION AFTER FILING OF AN APPLICATION BUT BEFORE FINAL**  
**REJECTION OR NOTICE OF ALLOWANCE OR CONCURRENTLY WITH A RULE**  
**1.114 RCE APPLICATION)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §§ 1.97 and 1.98, applicant(s) hereby submit(s) an Information Disclosure Statement for consideration by the Examiner.

I. LIST OF PATENTS, PUBLICATIONS OR OTHER INFORMATION

The patents, publications, or other information submitted for consideration by the Office are listed on the PTO-SB08(s), attached hereto.

II. COPIES

☒ a. Copies of cited U.S. patents and patent application publications are not included.  
Copies of foreign patent documents and non-patent literature are included.

☐ b. Some or all of the documents listed on the PTO-SB08 are not enclosed because they were cited in the International Search Report and copies should already be in the PTO file. If copies are needed, please contact the undersigned.

☐ c. REFERENCES PREVIOUSLY CITED OR SUBMITTED - Pursuant to 37 C.F.R. §1.98(d), consideration of information listed on the PTO-SB08 form(s) is requested since any patents, publications, or other information which are listed on the PTO-SB08 form(s) but for which copies are not enclosed herewith, were previously cited by or submitted to the PTO in one of the following applications which has been relied upon for an earlier filing date under 35 U.S.C. § 120:

U.S. Appl. No(s) and U.S. Filing Date

PCT/DK2004/000741 filed October 28, 2004

III. CONCISE EXPLANATION OF THE RELEVANCE

(check at least one box)

☐ a. DOCUMENTS IN THE ENGLISH LANGUAGE - The patents, publications, or other information listed on the attached PTO SB08 are in the English language and therefore, do not require a statement of relevancy.

☐ b. DOCUMENTS NOT IN THE ENGLISH LANGUAGE - A concise explanation of the relevance of all patents, publications, or other information listed that is not in the English language is as follows:

☒ c. ENGLISH LANGUAGE SEARCH REPORT - An English language version of the search report or action that indicates the degree of relevance found by the foreign office is attached, thereby satisfying the requirement for a concise explanation. See MPEP 609(III)(A)(3).

☐ d. OTHER - The following additional information is provided for the Examiner's consideration.

IV. FEES (check one box)

- ☐ a. This Information Disclosure Statement is being filed concurrently with the filing of a new patent application; therefore, no fee is required.
- ☐ b. This Information Disclosure Statement is being filed concurrent with the filing of a continuation-in-part, continuation, or divisional patent application; therefore, no fee is required.
- ☐ c. This Information Disclosure Statement is being filed within three months of the filing date of a national application (37 C.F.R. § 1.97(b)(1)). No fee or statement is required.  
*(This section is not to be used with RCE's.)*
- ☐ d. This Information Disclosure Statement is being filed within three months of the date of entry of the national stage as set forth in § 1.491 in an international application (37 C.F.R. § 1.97(b)(2)). No fee or statement is required.
- ☐ e. This Information Disclosure Statement is being filed concurrently with the filing of a Request for Continued Examination under § 1.114 (37 C.F.R. § 1.97(b)(4)). No fee or statement is required.
- ☒ f. This Information Disclosure Statement is being filed before the mailing date of a first Action on the merits (37 C.F.R. § 1.97(b)(3)). No fee or statement is required. In the event that a first Office Action on the merits has been issued, please consider this IDS under 37 C.F.R. § 1.97(c) and see the statement under 37 C.F.R. § 1.97(e) below, or, if no statement has been made, charge our deposit account for the fee as required by 37 C.F.R. § 1.17(p).
- ☐ g. This Information Disclosure Statement is being filed before the mailing date of a Final Office Action under 37 C.F.R. § 1.113 (See 37 C.F.R. § 1.97(c)(1)) or before the mailing date of a Notice of Allowance under 37 C.F.R. § 1.311 (See 37 C.F.R. § 1.97(c)(2)).
- ☐ No statement; therefore, a fee as required by 37 C.F.R. § 1.17(p) is attached.

or

☐ See the statement below. No fee is required.

V. STATEMENT UNDER 37 C.F.R. § 1.97(e)

(check only one box)

The undersigned hereby states that:

☐ a. Each item of information contained in the IDS was first cited in any communication from a foreign Patent Office in a counterpart foreign application not more than 30 days prior to the filing of this IDS; or

☐ b. Each item of information contained in the IDS was first cited in any communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS; or

☐ c. No item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of IDS was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of the IDS.

☐ d. Some of the items of information were cited in a communication from a foreign Patent Office. As to this information, the undersigned states that each item of information contained in the IDS was first cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS. As to the remaining information, the undersigned hereby states that no item of this remaining information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application and, to the best of my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this statement.

VI. PAYMENT OF FEES (check one box)

☐ The required fee is listed on the attached Fee Transmittal.

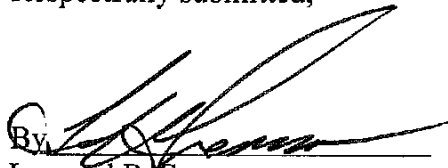
☒ No fee is required.

If the Examiner has any questions concerning this IDS, he/she is requested to contact the undersigned. If it is determined that this IDS has been filed under the wrong rule, the PTO is requested to consider this IDS under the proper rule and charge the appropriate fee to Deposit Account No. 02-2448.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

Dated: November 7, 2006

Respectfully submitted,



Leonard R. Svensson

Registration No.: 30,330

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Attorney for Applicant

Attachment(s):

- ☒ PTO-SB08
- ☒ Documents
- ☒ Foreign Search Report
- ☐ Fee
- ☐ Other:

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Substitute for form 1449/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Use as many sheets as necessary)</i>			<b>Complete if Known</b>		
			Application Number	10/577,489-Conf. #5111	
			Filing Date	April 27, 2006	
			First Named Inventor	Peter Birk RASMUSSEN	
			Art Unit	N/A	
			Examiner Name	Not Yet Assigned	
Sheet	1	of	3	Attorney Docket Number	4614-0197PUS1

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)					
	BA	WO-02/097044-A		12-05-2002			
	BB	WO-03/015812-A		02-27-2003			
	BC	WO-02/11759-A		02-14-2002			
	BD	WO-86/07383-A		12-18-1986			
	BE	JP-08 225462		09-03-1996	Toagosei Co Ltd		
	BF	JP-09 316000		12-09-1997	Toagosei Co Ltd		

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Examiner Signature		Date Considered	
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Sheet	2	of	3	Attorney Docket Number	4614-0197PUS1

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>	
	CA	WEI Y-Q et al., "Immunogene therapy of tumors with vaccine based Xenopus homologous vascular endothelial growth factor as a model antigen," Proceedings of the National Academy of Sciences of USA, National Academy of Science, Washington, US, vol. 98, no.20, 25 September 2001, pages 11545-11550		
	CB	FERRARA NAPOLEONE, "VEGF and the quest for tumor angiogenesis factors," Nature Reviews Cancer, vol. 2, no. 10, October 2002, pages 795-803		
	CC	Takahashi, Y. et al., "Expression of vascular endothelial growth factor and its receptor, KDR, correlates with vascularity, metastasis, and proliferation of human colon cancer," Cancer Research, 1995, Vol. 55, pg. 3964-3968.		
	CD	Tokunaga, T. et al., "Vascular endothelial growth factor (VEGF) mRNA isoform expression pattern is correlated with liver metastasis and poor prognosis in colon cancer," Br. J. Cancer, 1998, Vol. 77, Pgs. 998-1002.		
	CE	Kabbinavar, F. et al., "Phase II, randomized trial comparing bevacizumab plus fluorouracil (FU)/leucovorin (LV) with FU/LV alone in patients with metastatic colorectal cancer," J. Clin. Oncol., 2003, Vol. 21, pgs. 60-65.		
	CF	Prewett, M. et al., "Antivascular endothelial growth factor receptor (fetal liver kinase 1) monoclonal antibody inhibits tumor angiogenesis and growth of several mouse and human tumors," Cancer Research, 1999, Vol. 59, Pgs. 5209-5218.		
	CG	Zhu, Z. et al., "Inhibition of vascular endothelial growth factor-induced receptor activation with anti-kinase insert domain-containing receptor single-chain antibodies from a phage display library," Cancer Research, 1998, Vol. 58, Pgs. 3209-3214.		
	CH	Niethammer, A. G. et al., "A DNA vaccine against VEGF receptor 2 prevents effective angiogenesis and inhibits tumor growth," Nat. Med., 2002, Vol. 8, pgs. 1369-1375.		
	CI	Li, Y. et al., "Active immunization against the vascular endothelial growth factor receptor flk1 inhibits tumor angiogenesis and metastasis," J. Exp. Med., 2002, Vol. 195, Pgs. 1575-1584.		
	CJ	Stopeck, A. et al., "Results of a Phase I dose-escalating study of the antiangiogenic agent, SU5416, in patients with advanced malignancies," Clin. Cancer Res., 2002, Vol. 8, Pgs. 2798-2805.		
	CK	Devore, R. F. et al., "A randomized phase II trial comparing Rhumab VEGF (recombinant humanized monoclonal antibody to vascular endothelial cell growth factor) plus carboplatin/paclitaxel (CP) to CP alone in patients with stage IIIB/IV NSCLS," Proceedings of the American Society for Clinical Oncology, 2000, Vol. 19, Pg. 485a (Abstract).		
	CL	Yang, J. C. et al., "A randomized double-blind placebo-controlled trial of bevacizumab ( anti-VEGF antibody) demonstrating a prolongation in time to progression in patients with metastatic renal cancer," Proceedings of the American Society for Clinical Oncology, 2002, Vol. 21, Pg. 1 (Abstract).		
	CM	Smolich, B. D. et al., "The antiangiogenic protein kinase inhibitors SU5416 and SU6668 inhibit the SCF receptor (c-kit) in a human myeloid leukemia cell line in acute myeloid leukemia blasts," Blood, 2001, Vol. 97, Pgs. 1413-1421.		
	CN	Dias, S. et al., "Autocrine stimulation of VEGFR-2 activates human leukemic cell growth and migration," J. Clin. Invest., 2000, Vol. 106, Pgs. 511-521.		
	CO	Cross, M. J. et al., "VEGF-receptor signal transduction," Trends Biochem. Sci., 2003, Vol. 28, Pgs. 488-494.		
	CP	Muller, Y. A. et al., "The crystal structure of vascular endothelial growth factor (VEGF) refined		

Examiner Signature	Date Considered
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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

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Sheet	3	of	3	Attorney Docket Number	4614-0197PUS1

		to 1.93 Å resolution: multiple copy flexibility and receptor binding," Structure, 1997, Vol. 5, Pgs. 1325-1338.	
	CQ	Muller, Y. A. et al., "Vascular endothelial growth factor: crystal structure and functional mapping of the kinase domain receptor binding site," Proc. Natl. Sci. U.S.A., 1997, Vol. 94, Pgs. 7192-7197.	
	CR	Wiesmann, C. et al., "Crystal structure at 1.7 Å resolution of VEGF in complex with domain 2 of the Flt-1 receptor," Cell, 1997, Vol. 91, Pgs. 695-704.	
	CS	Wiesmann, C. et al., "Crystal structure of the complex between VEGF and a receptor-blocking peptide," Biochemistry, 1998, Vol. 37, Pgs. 17765-17772.	
	CT	Muller, Y. A. et al., "VEGF and the Fab fragment of a humanized antibody: crystal structure of the complex at 2.4 Å resolution and mutational analysis of the interface," Structure, 1998, Vol. 6, Pgs. 1153-1167.	
	CU	Fairbrother, W. J. et al., "Solution structure of the heparin-binding domain of vascular endothelial growth factor," Structure, 1998, Vol. 6, Pgs. 637-648.	
	CV	Christinger, H. W. et al., "Crystallization of the receptor binding domain of vascular endothelial growth factor," Proteins, 1996, Vol. 26, Pgs. 353-357.	
	CW	Starovasnik, M. A. et al., "Solution structure of the VEGF-binding domain of Flt-1: comparison of its free and bound states," J. Mol. Biol., 1999, Vol. 293, Pgs. 531-544.	
	CX	Fiebich, B. L. et al., "Synthesis and assembly of functionally active human vascular endothelial growth factor homodimers in insect cells," Eur. J. Biochem., 1993, Vol. 211, Pgs. 19-26.	
	CY	Ferrara, N. et al., "Expression of vascular endothelial growth factor does not promote transformation but confers a growth advantage in vivo to Chinese hamster ovary cells," J. Clin. Invest., 1993, Vol. 91, Pgs. 160-170.	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

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